REMARKS/ARGUMENTS

Upon entry of the current amendment, claims 1-35, 37, 39, 42-44, 46, 48, and 51-123 will be pending in the application, with claims 35, 37, 39, 42-44, 46, 48, 51, and 122-123 under examination. Claims 35, 37, 39, 44, 46, and 48 are hereby amended, claims 36, 38, 40-41, 45, 47, and 49-50 are hereby canceled, and new claims 122-123 are hereby added.

Support for the amendment to claim 35 can be found at, *e.g.*, original claim 36 and in paragraphs 0094, 0096, 0097, 0117, 0119 and 0120 of the published application. Claim 37 is amended to modify the claim dependency in light of the cancelation of claim 36, and to provide proper antecedent basis for "full length form of ATF6." Support for the amendment to claim 39 can be found at, *e.g.*, original claim 41. Support for the amendment to claim 44 can be found at, *e.g.*, original claim 45 and in paragraphs 0092, 0119 and 0136 of the published application. Claim 46 is amended to modify the claim dependency in light of the cancelation of claim 45, and to provide proper antecedent basis for "full length form of ATF6." Support for the amendment to claim 48 can be found at, *e.g.*, original claim 50. Support for new claims 122 and 123 can be found at, *e.g.*, paragraphs 0119 and 0120 of the published application, respectively. The amendments are made solely to advance prosecution of the application. No new matter is added.

Each of the Examiner's objections and rejections is addressed below in the order presented in the Office Action. Reference to paragraph numbering refers to the published application (US 2006/0246037 A1).

Objections to the Claims

The Examiner has objected to claims 35-51 on the grounds that independent claims 35 and 44 are drawn to "preventing cell death" without requiring any cell death to occur. *See* p. 2 of the Office Action. The Examiner also states that without a commensurate conclusion, the skilled artisan would not know if the claims are complete methods. *See* paragraph bridging pp. 2-3 of the Office Action. Finally, the Examiner objects to the punctuation in claim 36, and to claims 36-43 and 45-51 as depending from objected to base claims. *See* p. 3 of the Office Action.

Without agreeing with these objections, Applicants have amended independent claims 35 and 44 to clarify the scope of the presently claimed methods. Amended claim 35 recites a method for treating a disease characterized by neuronal cell death in a subject in need thereof in which administration of an ATF6 composition slows or arrests progression of the disease, or alleviates one or more symptoms of the disease, relative to the absence of treatment with ATF6. Amended claim 44 recites a method for preventing cell death in a population of cells in need thereof via administration of an ATF6 composition in which cell death that would otherwise occur from an accumulation of proteins is prevented relative to an absence of ATF6 administration. As amended, independent claims 35 and 44 provide a measure (*i.e.*, the absence of ATF6 administration) against which one could determine whether treatment of the disease, or prevention of cell death, is achieved. The amended claims also recite a conclusion, *i.e.*, slowing or arresting progression or alleviating symptoms of the disease (claim 35), and preventing cell death that would otherwise occur (claim 44). Applicants submit that these amendments, along with the cancelation of claim 36, address the Examiner's concerns, and respectfully request withdrawal of these claim objections.

Rejections under 35 U.S.C. 112, First Paragraph – Written Description

The Examiner has rejected claims 35-51 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserts that the claims are drawn to a generic functional form of ATF6, which includes functional mutant and derivative forms with various deletions, additions or amino acid substitutions. *See* pp. 3-4 of the Office Action. The Examiner asserts that neither the art nor the application indicates which regions of ATF6 are required to maintain function and that without this information the skilled artisan could not have concluded that Applicants were in possession of the breadth of generic modifications embraced by the claims. *See* p. 4 of the Office Action.

Without agreeing with the basis of the rejection, Applicants have amended independent claims 35 and 44 to recite a functional form of ATF6 selected from a full-length form of ATF6, an N-terminal domain form of ATF6, a bZIP-ATF6 fragment, and combinations thereof, and have deleted reference to functional derivatives of ATF6. These forms of ATF6 are

described in the application with sufficient identifying structural characteristics such that a skilled artisan would have concluded that Applicants were in possession of the claimed invention as of the priority date of the application. The full-length form of ATF6 is described in the application at paragraph 0081, and in Figures 1-4 of the application. The N-terminal domain and bZIP-ATF6 fragment forms are described in paragraphs 0144 and 0145 of the application. Thus, the claimed invention is described in the application in compliance with the written description requirement. The rejection of dependent claims is addressed by the amendments to independent claims 35 and 44.

Based on the foregoing, Applicants respectfully request withdrawal of this ground of rejection.

Rejections under 35 U.S.C. 112, First Paragraph - Enablement

The Examiner has rejected claims 35-51 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner asserts that the claims are drawn to methods of inhibiting cell death, caused by any mechanism, by administration of any one of a plethora of ATF6 proteins, but that neither the art nor the application provides any evidence that ATF6, or of which forms of ATF6, will provide inhibition of cell death in any particular context. *See* pp. 4-5 of the Office Action.

Without agreeing with the basis of the rejection, Applicants have amended independent claims 35 and 44 to recite, respectively, treatment of a disease associated with abnormal precipitation or accumulation of proteins, and prevention of cell death that would otherwise occur from an undesired accumulation of proteins. Thus, as amended, the presently claimed invention is directed to treating disease or preventing cell death caused by a single mechanism, *i.e.*, an abnormal accumulation of proteins. The claims have also been amended, as discussed above with regard to the written description requirement, to recite specifically defined forms of ATF6. An accumulation of unfolded proteins triggers the unfolded protein response. *See* paragraph 0016. As acknowledged by the Examiner (*see* p. 5, last paragraph of the Office Action) and as described in the specification (*see* paragraph 0018), expression of ATF6 is associated with the unfolded protein response. Based on Applicants' discovery that

overexpression of ATF6 in a cell prevents cell death that would otherwise occur when an undesired accumulation of proteins occurs in the cell (*see* paragraph 0119), the skilled artisan could practice the claimed methods without undue experimentation. Thus, the claimed invention, as recited in the amended claims, is enabled by the specification.

Based on the foregoing, Applicants respectfully request withdrawal of this ground of rejection.

Rejections under 35 U.S.C. 103(a)

The Examiner has rejected claims 44-51 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 6,635,751 to Haze et al. (or alternatively WO 2000/29429 to Haze et al.).

Applicants respectfully traverse. Amended claim 44 recites a method for preventing cell death in a population of cells via administration of an ATF6 composition, wherein cell death that would otherwise occur from an undesired accumulation of proteins is prevented relative to the absence of ATF6 administration.

Haze et al. discusses transformation of a yeast cell with a plasmid containing a nucleic acid encoding ATF6. *See* Example 2, columns 22-23. The transformation with ATF6 discussed in Example 2 is performed as 1 of 4,300,000 transformations to screen a human lymphocyte cDNA library to identify clones in which transcription of a reporter gene increased in an endoplasmic reticulum stress-response element-dependent manner. *See* col. 22, lines 38-48. Haze et al. does not discuss or suggest administration of a functional form of ATF6 to a population of cells ***in need thereof***, as recited in independent claim 44, nor ***preventing cell death that would otherwise occur*** from an undesired accumulation of proteins, as claimed. As articulated by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396, and as set forth in the *Examination Guidelines for Determining Obviousness under 35 U.S.C. 103* (Fed. Reg. Vol. 72, No. 195, paragraph bridging pp. 57528-57529), "rejections on obviousness cannot be sustained by mere conclusory statements; instead there must be some articulated reasoning with some rationale underpinning to support the legal conclusion of obviousness." Because the Examiner has failed to provide any rationale by which a skilled

artisan would have been motivated to modify Haze et al. to arrive at the claimed invention, the Examiner has failed to set forth a *prima facie* case of obviousness. Thus, the claimed invention, as set forth in independent claim 44, and claims depending therefrom, is patentable over the cited art.

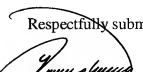
Based on the foregoing, Applicants respectfully request withdrawal of this ground of rejection.

It is noted that no art rejection has been made against claims 35-51. Therefore, it is assumed that claims 35, 37, 39, 42 and 43, which remain pending in the application, are free of the art.

New claims 122 and 123 are patentable for at least the same reasons discussed above.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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